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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,759	10/23/2001	Krzysztof B. Wicher	2739-2001-001	8401

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,759	WICHER ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-15 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-15 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Claims 1-3, 7-15, 17-22 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 10-15-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 15 and claims 2-3 and 17-20 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 15 are directed to "isolated nucleic acid molecule....and encoded by the amino acids of SEQ ID NO:2". It is well understood in the art that nucleic acid sequence "encodes" and amino acid sequence but not the other way round. Therefore the claim as written is unclear or indefinite. It appears that applicants intended to recite " and encodes (or encoding) the amino acid sequence SEQ ID NO:2". If this is so amending the claim accordingly would overcome the above rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 15, 17-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 and claim 15 as amended recite the phrase "wherein said polypeptide is more soluble". However, a perusal of the specification indicates that applicants have no support for "a polypeptide that is more soluble" which now constitutes a "new matter". Therefore claims 1 and 15 and claims 2-3 and 17-20 which depend from claim 1 and 15 respectively are rejected for introducing "new matter" into the claims. A perusal of the specification at specific pages and line numbers which applicants have remarked as providing support for the above amendment did not indicate support for the above phrase. Applicants are required to delete the subject matter that is indicated as "new matter".

Claims 7-14, 21-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules wherein the genus comprises fragments of SEQ ID NO:3.

The specification does not contain any disclosure of the function of all DNA sequences that are fragments of SEQ ID NO:3. The genus of cDNAs that comprise these above cDNA molecules is a large variable genus with the potentiality of encoding proteins with varied functions. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus, i.e., SEQ ID NO:3 as encoding a cellulase which is insufficient to put one

of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

It is not clear to the Examiner as to why applicants amended the claims by deleting the functional language from the above claims. Reinstating the functional language in the claims would overcome this rejection.

Claims 15, 17-20, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence with SEQ ID NO:3 encoding a polypeptide with SEQ ID NO:2 having thermostable cellulase activity, does not reasonably provide enablement for any variant DNA sequence that encodes a polypeptide whose amino acid sequence is 85% identical to the amino acid sequence of SEQ ID NO:2 or encoding such polypeptide that is further truncated by one or more amino acid residues corresponding to position one to about position 40 in SEQ ID NO:2, including vectors, host cells comprising such DNA and method of making such truncated polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 15, 17-20 are so broad as to encompass any DNA, which encodes a variant glycosylhydrolase, polypeptide whose amino acid sequence is 85% identical to the amino acid sequence of SEQ ID NO:2 and is further truncated such that one or more amino acid residues corresponding to position one to about position 40 in SEQ ID NO:2 are deleted. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above polynucleotides for the process of producing recombinant protein with improved characteristics. Therefore changing the nucleotide sequences as proposed by the applicants (i.e., a polynucleotide encoding a polypeptide that is 85% identical to SEQ ID NO:2 and is further truncated such that one or more amino acid residues corresponding to position one to about position 40 in SEQ ID NO:2 are deleted) may not lead to desired function of the polynucleotides. It would require undue experimentation of the skilled artisan to make the claimed polynucleotides. The specification is limited to teaching the making of the polynucleotide with SEQ ID NO:3 to encode a polypeptide with SEQ ID NO:2 in which specific N-terminal amino acids are deleted, but provides no guidance with regard to making and using of polynucleotides that encode a polypeptide that is 85% identical to SEQ ID NO:2. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides that encode a polypeptide that is 85% identical to SEQ ID NO:3, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polynucleotides encompassed

(i.e., polynucleotides that encode a polypeptide that is 85% identical to SEQ ID NO:2) by the claims. It would be an undue burden to those skilled in the art to determine where in SEQ ID NO:2, specific amino acid/s needs to be altered in order to arrive at polypeptides that is 85% identical to SEQ ID NO:2. However, in this case the disclosure is limited to a single nucleotide encoding a single polypeptide with SEQ ID NO:2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence that can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of DNA encoding a protein having thermostable cellulase activity because the specification does not establish: (A) a rational and predictable scheme for modifying any amino acid of the thermostable cellulase with an expectation of obtaining the desired biological function and utility; (B) the general tolerance of the thermostable cellulase amino acid/DNA sequence to modification and extent of such tolerance; (C); the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any variant DNA sequence that encodes a polypeptide whose amino acid sequence is 85% identical to the amino acid sequence of SEQ ID NO:2. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher, 166*

USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants indicate that they have deleted the recitation of "85% sequence identity". While such a deletion is explicit in claim 1 (by strike through), applicants have retained the phrase in claim 15 in square brackets. Therefore, it is not clear to the Examiner as to what applicants have intended to do in claim 15. For examination purposes, Examiner has concluded that the above phrase continues to be part of claim 15 and therefore has maintained the above rejection.

Examiner has withdrawn the previous rejection of claims 1-22 and 30 under 35 U.S.C. 103(a) as obvious over Halldorsdottir et al. (Appl. Microbiol. Biotechnol., 1998, Vol. 49:277-284, and the enclosed sequence alignment), and Ohmiya et al. (J. Bacteriol., 1991, Vol. 173(2):636-641) in view of arguments provided by the applicants and also due to the fact that applicants are claiming a polynucleotide encoding a polypeptide.

Conclusion

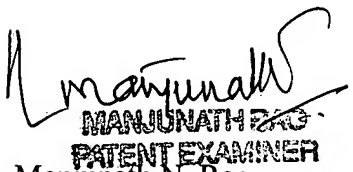
None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
January 5, 2004